DHSS HEALTH ALERT

Date: May 11th, 2023

The Missouri Department of Health & Senior Services (DHSS) uses four types of documents to provide important information to medical and public health professionals, and to other interested persons:

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Phone: 800-392-0272
Fax: 573-751-6041
Web: health.mo.gov

FROM: Paula F. Nickelson, Acting Director

SUBJECT: Xylazine-Involved Fatal Drug Overdoses in Missouri, 2019-2022

Xylazine is used in veterinary medicine as a sedative and muscle relaxant, but it is not approved by the Food and Drug Administration (FDA) for use in humans. Persons who use xylazine-adulterated opioids are at high-risk for fatal overdose. The White House Office of National Drug Control Policy declared xylazine and the use of fentanyl adulterated or associated with xylazine (FAAX) an emerging threat on April 12, 2023. Missouri DHSS detected a sharp increase in xylazine involved deaths in Missouri from 39 deaths in 2021 to 109 deaths in 2022, a 180% increase. Nearly two thirds (65%) of those deaths occurred in adults between 25 and 44 years of age. For all xylazine-involved deaths in 2019-2022, synthetic opioids were also found in 99.4% of these deaths. Increased surveillance and public education, as well as expanded postmortem testing for xylazine is needed, especially in Missouri jurisdictions with a high prevalence of fentanyl use.

Xylazine is an α-2 agonist similar to clonidine, lofexidine, and dexmedetomidine. It is used in veterinary practice as a sedative and analgesic. Xylazine is not FDA approved for human use and is not controlled under the federal Controlled Substances Act (CSA). This non-opioid agent is increasingly being found in combination with opioids such as fentanyl. Xylazine is known as “tranq” or “tranq dope” in the illicit drug market. The drug’s reported duration of effect is longer than that of fentanyl; therefore, it may enhance the euphoria and analgesia induced by fentanyl and reduces the frequency of injections. Recreational use of xylazine can occur via oral ingestion, smoking, snorting, or intramuscular, subcutaneous, or intravenous injection (most common). When used in combination with an opioid, such as heroin or fentanyl, xylazine may worsen respiratory depression during the drug overdose.

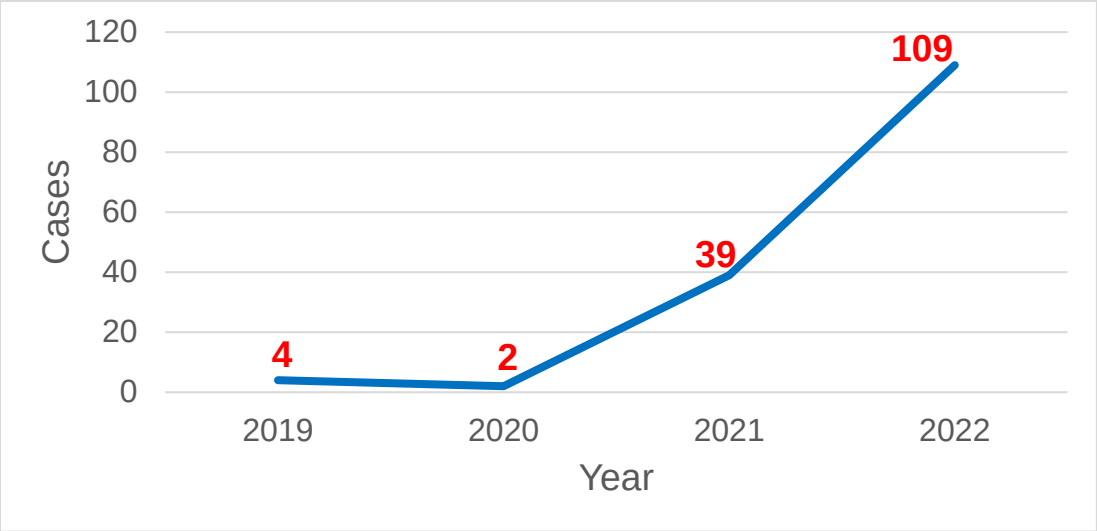
Xylazine was found in over 90% of illicit drug samples tested in Philadelphia in 2021 (1). As of March 2023, fentanyl mixed with xylazine had been found in drug seizures in 48 states (2). According to the CDC, the estimated number of drug-poisoning deaths in the United States involving xylazine went from 260 in 2018 to 3480 in 2021, a 1238%

increase (2). The analysis published in MMWR found that among 45,676 overdose deaths reported from 38 states and the District of Columbia in 2019, xylazine was detected in 1.8% of the deaths, and xylazine was listed as a cause of death in 64.3% of deaths in which it was detected (3). In a Cook County, IL study, fentanyl or fentanyl analogs were detected on forensic testing in most xylazine-involved deaths (99.2%). Other common co-occurring substances included diphenhydramine (79.7%), cocaine (41.1%), and quinine (37.3%) (4). Many coroners and medical examiners may not include xylazine in their routine toxicology testing which would leave it largely undetected when investigating cause of death.

Xylazine Involved Deaths in Missouri

A sharp increases in xylazine-associated deaths were observed in Missouri in 2021 and 2022 (Figure 1.). Among death cases, 73% were males. Nearly two third (65%) of xylazine involved deaths occurred in adults between 25 and 44 years of age (Figure 2.). Four adjacent Missouri jurisdictions (St Louis City, St Louis, St Charles, and Jefferson counties) comprise 86% of death cases during the 2019-2022 time period. It is likely that better availability of xylazine testing in the St Louis metropolitan area is contributing to those jurisdictions being overrepresented. For all xylazine-involved deaths in 2019-2022, synthetic opioids were also found in 99.4% of these deaths. Improved availability of xylazine testing in the recent years could be contributing to the sharp increase of xylazine associated death reports in 2021 and 2022.

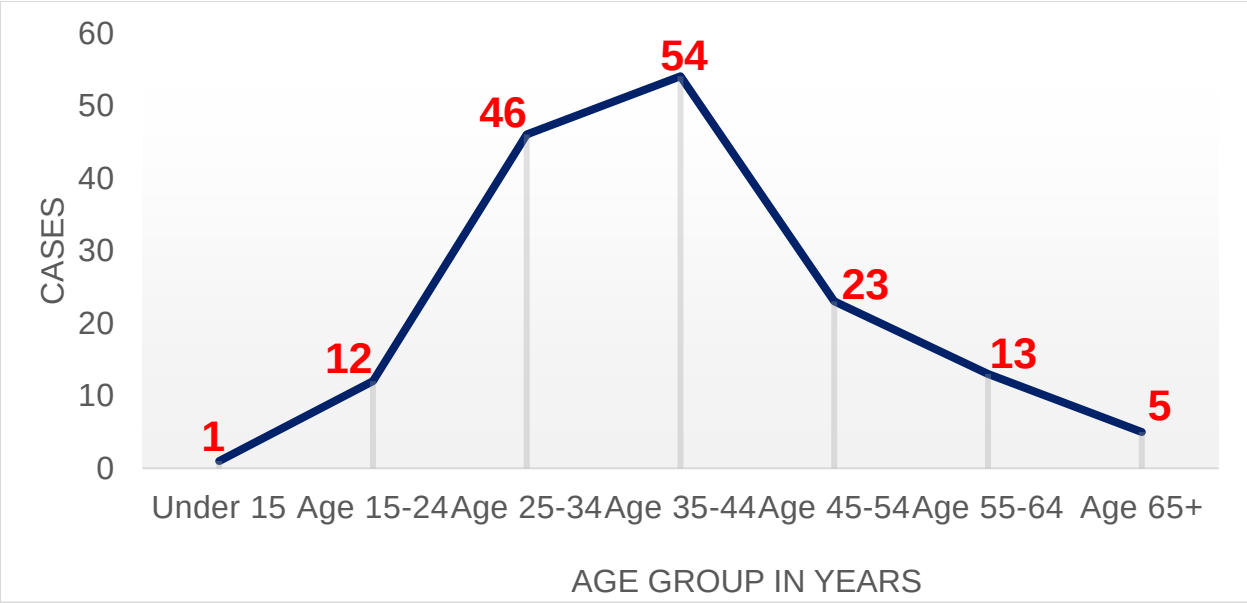
Figure 1. Drug Overdose Deaths Involving Xylazine, Missouri, 2019-2022* **



* Xylazine involved deaths include deaths where ‘xylazine’ was found in the literal text field on the death certificate.

** Source: Missouri Vital Statistics, 2022 data is provisional

Figure 2. Drug Overdose Deaths Involving Xylazine, by Age Group, Missouri, 2019-2022* **



* Xylazine involved deaths include deaths where 'xylazine' was found in the literal text field on the death certificate.

** Source: Missouri Vital Statistics, 2022 data is provisional

Clinical Information

As a centrally acting α2 -agonist medication, xylazine inhibits the release of norepinephrine and epinephrine. The effects on the central nervous system include sedation, analgesia, and euphoria. Reduced sympathetic outflow from the central nervous system causes decreased peripheral vascular resistance, heart rate, and blood pressure. All routes of exposure to xylazine have been associated with drowsiness or coma, and in rare instances, apnea and death. Xylazine also causes decreased sensitivity to pain, respiratory depression, bradycardia (low heart rate), hypotension (low blood pressure), and potentially hypothermia. After taking xylazine with an opioid, a person may experience bradycardia and hypotension not explained by heroin or fentanyl alone. Respiratory depression reported in people using xylazine is likely due to the drug increasing the risk of opioid-induced respiratory depression. Xylazine can cause severe circulatory changes with peripheral vasoconstriction leading to poor tissue perfusion, skin ulceration, and necrosis. People who inject drugs containing xylazine can develop severe skin wounds and patches of dead and rotting tissue that easily become infected and, if left untreated, may lead to amputation (Picture 1.). These wounds can develop in areas of the body away from the injection site and may become life-threatening. Soft tissue infections at injection sites and loss of digits have been reported

as well. Because xylazine's duration of effect is longer than that of fentanyl or heroin, repeated intake may allow xylazine levels to accumulate.

Picture 1. Xylazine-associated Skin Injury (N Engl J Med. 2023 Apr 26)

People who use xylazine may develop dependence, and have severe withdrawal symptoms, such as irritability, anxiety, and dysphoria when the drug is stopped abruptly. Severe xylazine withdrawal symptoms are unlikely to be managed by medications for opioid use disorder (MOUD) (i.e., methadone, buprenorphine, or naltrexone). Limited data are available for clinical management of the xylazine withdrawal in inpatient settings. Therefore, xylazine presents new potential public health challenges associated with possible withdrawal signs and symptoms in those with xylazine-related substance use disorder.

Routine toxicology tests do not test for xylazine. It may therefore be under-detected and under-accounted for in overdose cases and other life-threatening events. Since xylazine is not an opioid, it does not respond to naloxone, and there is no antidote or reversal agent for xylazine. Even though naloxone is not effective in treating drug overdoses caused solely by non-opioids, such as xylazine, the administration of naloxone may be helpful in drug overdoses caused by a combination of xylazine and opioids like fentanyl and its analogues. Therefore, when a patient presents with a possible exposure to xylazine, practitioners should provide routine care for opioid intoxication, particularly the administration of naloxone, as indicated. The treatment for overdoses involving xylazine is supportive: airway maintenance, breathing

and circulation support, and infusion of IV fluids. If indicated, early administration of atropine may mitigate the onset or severity of bradycardia.

Recommendations

- Public education, especially among people who use illicit drugs, regarding the possible presence of xylazine in illicit drugs and the need for emergency medical care even when naloxone is administered.
- Any individual suspected of consuming substances containing xylazine should receive counseling about the dangers of this substance and extensive advice on harm reduction.
- Because xylazine is most often mixed with opioids, the individual exposed to xylazine should also be offered access to medications for opioid use disorder (MOUD) (i.e., methadone, buprenorphine, or naltrexone) and referral to treatment to reduce opioid overdose risk.
- Health care providers should consider the presence of xylazine when managing drug overdose, especially when naloxone administration is ineffective.
- Expand postmortem testing for xylazine and co-occurring substances in opioid-related deaths.
- While routine toxicology tests do not test for xylazine, local jurisdictions may establish partnerships with toxicology laboratories that can identify xylazine in drug or biologic samples.

For questions on management of these patients, contact the **Missouri Poison Center (1-800-222-1222)**

References

1. Philadelphia Department of Public Health. Substance use Philly: xylazine. (https://www . substanceusephilly . com/ tranq).
2. Gupta R, Holtgrave DR, Ashburn MA. Xylazine - Medical and Public Health Imperatives. N Engl J Med. 2023 Apr 26. doi: 10.1056/NEJMp2303120. Epub ahead of print. PMID: 37099338.
3. Kariisa M, Patel P, Smith H, Bitting J. Notes from the Field: Xylazine Detection and Involvement in Drug Overdose Deaths - United States, 2019. MMWR Morb Mortal Wkly Rep. 2021 Sep 17;70(37):1300-1302. doi: 10.15585/mmwr.mm7037a4. PMID: 34529640; PMCID: PMC8445380.
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HEALTH ALERT

Missouri Department of Health and Senior Services

Paula F. Nickelson, Director **6 December 2023**

Emerging *Candida auris* Infection Cases in Missouri Health Care Facilities

The Missouri Department of Health & Senior Services (DHSS) uses four types of documents to provide important information to medical and public health professionals, and to other interested persons:

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Summary

- In recent weeks, the Missouri Department of Health and Senior Services (DHSS) has detected cases of *Candida auris* (*C. auris*) within health care facilities in the Saint Louis Metro area. The state of Missouri previously had no prevalence of locally acquired *C. auris* infection.
- To prevent spread throughout the state's health care facilities, this health alert provides background and epidemiological information on *C. auris*, and describes recommendations for facilities regarding infection prevention and control, transmission-based precautions, inter-facility communications, screening, laboratory testing, and reporting requirements.

C. auris Background

C. auris is an emerging multi-drug resistant yeast that was discovered in 2009 in Asia, and has since spread worldwide. The earliest known case in the United States was in 2013. Due to resistance to many antifungal drugs, *C. auris* is considered an urgent antimicrobial resistance threat by the Centers for Disease Control and Prevention (CDC). *C. auris* spreads easily in health care settings and is difficult to treat due to drug-resistance. Invasive infections with *C. auris* are particularly concerning and have caused death in about one in three persons who developed severe disease due to this infection.

According to the CDC *C. auris* tracking tool, there were 2,377 clinical cases and 5,754 colonization/screening cases identified from January 2022 – December 2022 across 29 states. **Clinical cases** are based on cultures or culture-independent diagnostic testing from specimens collected during the course of clinical care for the purpose of diagnosing or treating disease. **Colonization/screening cases** are identified when swabs are collected from patients to determine whether they may be carrying the organism somewhere on their bodies without active signs of infection.

Risk Factors

C. auris mostly affects individuals with severe underlying conditions, those requiring complex medical care, as well as those with indwelling devices. Patients with invasive medical devices like breathing tubes, feeding tubes, catheters in a vein, or urinary catheters tend to be at increased risk for acquiring *C. auris* infection. Healthy people without these risk factors, including health care workers and family members, have a low risk for becoming infected with *C. auris*.

Transmission
C. auris can spread from one patient to another in hospitals, nursing homes, and other health care settings. People can be colonized with *C. auris* without displaying any symptoms but, without proper infection control practices, still transmit the infection to other persons. It can spread through close contact with affected patients and contaminated surfaces or equipment. *C. auris* can live on surfaces for several weeks. Contact with these surfaces allows the fungus to spread to other people. Once a patient has tested positive for *C. auris* infection or colonization, they are considered colonized for life and infection control measures should be utilized.

Symptoms and Colonization
C. auris can cause infections in different parts of the body such as in the bloodstream, open wounds, and ears. The symptoms depend on the location and severity of *C. auris* infection. Symptoms may be similar to symptoms of an infection caused by bacteria. There is not a common set of symptoms specific for *C. auris* infections. People can get *C. auris* on their skin and other body sites without getting sick or having an active infection with symptoms. Health care providers may refer to this as 'colonization.' Someone who is colonized can still contaminate surfaces or objects they contact with *C. auris*, which can then spread it to other patients.

Diagnosis
Health care Providers can diagnose a patient as actively infected or colonized with *C. auris* in two ways:

- **Colonization screening–** a health care provider swabs the patient's skin by rubbing a swab near the armpits and groin and sends the swab to a laboratory for testing.
- **Clinical specimen testing–** If a patient is showing symptoms of an infection of an unknown cause, a health care provider may collect a clinical sample, like blood or urine. They usually test for many types of infections, including those caused by bacteria, and the results may show that the patient has *C. auris*.

Retesting patients infected or colonized with C. auris is not recommended and should not be used to change infection control measures. A negative test after a previous positive does not ensure that the patient no longer has C. auris on their skin or other body sites and will not spread it to others.

Treatment
Some *C. auris* strains have been resistant to all three main classes of antifungal medicines, meaning none are able to treat the infection. In this situation, multiple antifungal medicines or newer antifungals may be used to treat the infection. Most strains of *C. auris* found in the United States have been susceptible to echinocandins, although reports of echinocandin-resistant (or pan-resistant) cases are increasing. Patients who are colonized (have *C. auris* detected on their body but do not have symptoms of infection) should not be treated with antifungals for *C. auris*. There is no evidence this prevents future illness.

Epidemiology of C. auris in Missouri

C. auris was first seen in Missouri in late 2020. Until this most recent increase in cases, there were only two cases reported in Missouri and both had acquired infection in other states with known high incidence of *C. auris*. Since October 2023, Missouri DHSS has detected eight additional cases of *C. auris* with the majority in the St. Louis Metro area.

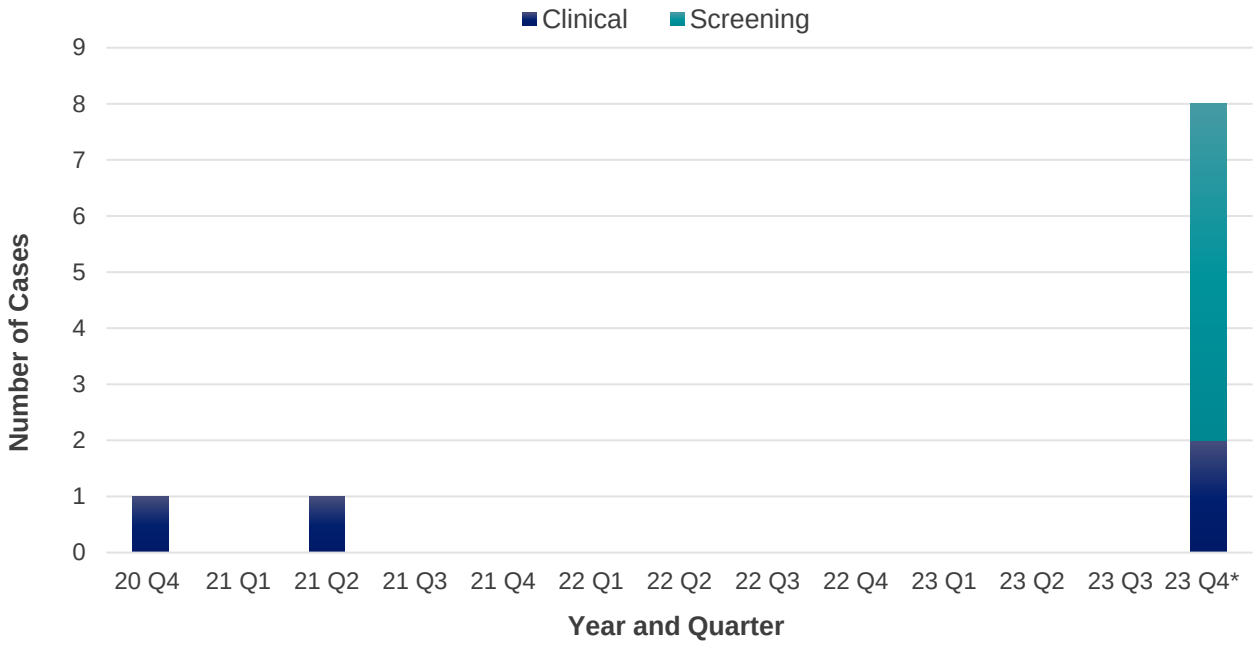
At least one *C. auris* infection case has been detected in a variety of health care facilities including: Acute Care Hospitals, Skilled Nursing Facilities, and Rehabilitation Hospitals. Currently, there are at least three local health jurisdictions with one or more positive cases. These recent cases are of concern since they mark the first presumed instances of local transmission within the state of Missouri.

Recent cases have largely been identified through point prevalence surveys (PPS) conducted by health care facilities as part of epidemiologic investigation and public health surveillance. Colonized individuals have been detected via axilla/groin swabs, and clinical cases have been identified from positive tests of blood, bile, and wounds.

From the 10 cases reported in Missouri:

- Patient age ranges from 36 to 83 with a median age of 67.
- Three patients reported receiving health care in geographic areas with a high *C. auris* incidence.
- All patients reported to have history of complex medical care (including invasive medical devices, wounds, and underlying conditions).
- All patients currently infected or colonized with *C. auris* resided in a skilled nursing facility or have had hospitalizations within the last 12 months.

Graph. Number of *C. auris* cases detected in Missouri by quarter from Q4 2020 – Q4 2023*



*23 Q4 data is preliminary as of 11/30/2023

Missouri DHSS Recommendations

Infection Prevention and Control

The CDC and the Missouri DHSS recommends health care facilities take the following actions to identify and control further spread:

- Immediately initiate and regularly reinforce appropriate use of transmission-based precautions based on the setting (described below).
- Inform and educate appropriate personnel about the presence of a patient with *C. auris* and the need for rigorous adherence to infection control practices.
- Ensure strict adherence to hand hygiene and appropriate personal protective equipment (PPE) use. Alcohol-based hand sanitizer is effective against *C. auris* and is the preferred method for cleaning hands when they are not visibly soiled. Wearing gloves is not a substitute for hand hygiene.
- Perform thorough cleaning and disinfection of the patient care environment and any shared equipment (daily and terminal cleaning) used by patients with confirmed or suspected *C. auris.* Use a disinfectant active against *C. auris* identified by the Environmental Protection Agency (EPA) from EPA List P.
- If possible, use dedicated medical equipment for patients with confirmed or suspected *C. auris*.
- Promote antimicrobial stewardship to limit the emergence of *C. auris* and other multi-drug resistant organisms (MDROs).

Transmission-Based Precautions

Health care facilities should not decline admission based on colonization or presence of MDRO infection including *C. auris*. All patients with *C. auris* infection or colonization should be placed on the appropriate transmission based precautions based on the setting:

- **Acute care hospitals, post-acute care facilities (including long-term acute care hospitals)** should place patients with *C. auris* on contact precautions.
- **Skilled Nursing Facilities** should place patients on Enhanced Barrier Precautions (when contact precautions do not otherwise apply). More information on enhanced barrier precautions can be found here: https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html
    - **Skilled nursing facilities with ventilator units,** should initially place patients on contact precautions. Patients may be able to be moved to Enhanced Barrier Precautions.
- **Dialysis clinics and providers** should care for patients with *C. auris* by having health care personnel wear disposable gowns and gloves during patient care or when touching items at the dialysis station. Gowns and gloves should be removed and disposed of carefully, and hand hygiene should be performed when leaving the patient's station. Minimize exposure to other patients by placing the patient away from others or seeing the patient at the end of day.
- **Outpatient Settings** should care for patients with *C. auris* by having health care personnel wear disposable gown and gloves if extensive patient contact is anticipated or contact with infected areas is planned (e.g., debridement or dressing of colonized or infected wound). Gowns and gloves should be removed and disposed of appropriately, and hand hygiene should be performed when leaving the patient's room.
- **Home Health care settings** should care for patients with *C. auris* by having health care personnel wear disposable gown and gloves when entering the area of the home where providing patient care. Gowns and gloves should be removed and disposed of appropriately. Hand hygiene should be performed when leaving the patient care area. Minimize exposure to other patients by seeing the patient at the end of day.

Place all patients with confirmed or suspected *C. auris* infection or colonization in a private room. If a private room is not available:

- Patients infected or colonized with *C. auris* and/or other MDROs should be placed in rooms with patients colonized with the same organism(s). CDC does not recommend placing patients with *C. auris* in rooms with patients who have other types of MDROs.
- Avoid placing *C. auris* patients with patients who have indwelling devices (e.g., central venous catheter, tracheostomy tubes and mechanical ventilators), serious underlying medical conditions, or are otherwise immunocompromised.

Missouri DHSS does not currently recommend the discontinuation of precautions for a patient or resident with a current or past history or *C. auris* colonization or infection.

Interfacility Communication

Robust communication at the time of transfer ensures the continuation of infection prevention and control measures during transitions of care. This can be accomplished via verbal report at the time of transfer, in the discharge summary, or through the use of an interfacility transfer tool.

- Upon admission, ask about a patient's *C. auris* and other MDRO status, if not included in the accompanying medical records.
- Upon admission, assess *C. auris* and other MDRO status for all patients by reviewing medical records and utilizing EHR or HL7, especially for patients being admitted from long term acute care hospitals or from ventilator units.
- Upon discharge, communicate a patient's *C. auris* and other MDRO status, including for any patients screened for an MDRO, but for whom laboratory results are not available at the time of transfer, to any receiving health care facility prior to transfer.
    - This should be done by including a written notification of the infection or colonization to the receiving facility in transfer documents. The referring facility should ensure that the documentation is readily accessible to all parties involved in patient transfer (for example,

referring facility, medical transport, emergency department, receiving facility). CDC has a sample Interfacility Transfer Form that facilities can use.

Containment Response
A single case of *C. auris* (active infection or colonization) requires a robust containment response. Be aware that as part of the current investigation the DHSS Healthcare Associated Infections/Antimicrobial Resistance (HAI/AR) Program may be conducting outreach to health care facilities and clinical laboratories with epidemiologic links to case patients or health care facilities with cases of *C. auris* infection.

Colonization Screening[1]
Missouri DHSS recommends screening patients for *C. auris* who meet any of the following criteria:

- Patients presenting from long-term acute care facilities, skilled nursing facilities, or rehabilitation facilities who, within the past 12 months, have history of
  - Multi-drug resistant organisms (MDROs)
  - Mechanical ventilation or tracheostomy
  - Chronic or unhealing wounds
- Patients hospitalized outside of the United States within the preceding 12 months
- Residents of Illinois with extended stays in health care facilities (acute care and long-term care) due to recent incidence of *C. auris* in this area
- Residents of states with historically high incidence of *C. auris*, who also have extended stays in health care facilities (acute care and long-term care)

Testing of the environment or equipment for *C. auris* is not routinely recommended. Likewise, testing of health care workers or family members who care for patients with *C. auris* (or an exposure to *C. auris*) is not routinely recommended.

Clinical Laboratories
Clinical laboratories processing specimens from residents receiving health care in Missouri should implement methods to detect *C. auris* as outlined below:

- Use the CDC *Candida auris* laboratory resource and algorithm to identify *C. auris* based on the available phenotypic laboratory method and initial species identification.
- If your laboratory does not have methodologies required to speciate *C. auris*, talk with the HAI/AR Program to evaluate the utility of forwarding isolates suspicious for *C. auris* for further testing at commercial or public health laboratories that can perform *C. auris* identification. Please forward any positive *C. auris* isolates to the Missouri State Public Health Laboratory (MSPHL).
- If possible, perform speciation for all yeast isolates from an inpatient in a health care facility (acute care hospital, LTACH, or SNF), including from both normally sterile and nonsterile body sites. This activity may be particularly useful in the three months following the release of this alert, as we seek to understand the local epidemiology of *C. auris* in Missouri.
- CDC recommends that all yeast isolates obtained from a normally sterile site be identified to the species level so appropriate initial treatment can be administered based on the typical, species-specific susceptibility patterns.
- Species-level identification of *Candida* isolates from non-sterile sites should be conducted in the following circumstances:
  - If clinically indicated in the care of the patient.
  - To detect additional colonized patients when a case of *C. auris* infection or colonization has been detected in a facility or unit.

[1] Colonization testing (screening) for *C. auris* and carbapenem-resistant bacteria is available at no cost through the CDC Antimicrobial Resistance Laboratory Network. These services can be accessed in consultation with the MO DHSS by contacting the Healthcare Associated Infections/Antimicrobial Resistance (HAI/AR) Program.

- If the patient has had an overnight stay in a health care facility within an identified domestic hotspot, or outside the U.S. in the previous year, especially in a country or region with documented *C. auris* transmission.
- If the patient currently or previously resided in skilled nursing facilities with ventilated patients or in long term acute care hospitals.

Reporting

Health care facilities, providers and laboratories with suspected or confirmed cases of *C. auris* (active infection or colonization), should report them to the DHSS HAI/AR Program at 573-751-6113 or the DHSS Emergency Response Center (ERC) at 800-392-0272. *C. auris* is implicitly reportable in Missouri as an emerging or unusual disease per the Regulatory Documentations of Reportable Diseases and Conditions in Missouri (19 CSR 20-20.020). *C. auris* became nationally notifiable in 2018.

Please contact the Missouri DHSS HAI/AR Program for:

- Patients newly colonized or infected with *C. auris* (immediately notifiable)
- Guidance on *C. auris* screening of roommates or other close contacts
- Guidance on patient cohorting (i.e., grouping patients infected with the same infectious agents together to confine their care to one area and prevent contact with susceptible patients)
- Guidance of infection control interventions
- HAI Surveillance including reporting, specimen collection, and specimen submission to the Missouri State Public Health Laboratory (MSPHL).

The Missouri DHSS HAI/AR Program can be contacted at the following email address: info@health.mo.gov

References

Worsening Spread of *Candida auris* in the United States, 2019 to 2021 | Annals of Internal Medicine (acpjournals.org)
CDC *C. auris* Homepage
Infection Prevention and Control for *Candida auris*
EPA List P
Implementation of Personal Protective Equipment (PPE) Use in Nursing Homes to Prevent Spread of Multidrug-resistant Organisms (MDROs) | HAI | CDC
Identification of *Candida auris* | *Candida auris* | Fungal Diseases | CDC

Target Audience

Local Health Departments, Infectious Disease Physicians, Hospital Emergency Departments, Infection Control Preventionists, Health Care Providers, Long Term Care Facilities, and Laboratories

Author

DHSS Healthcare Associated Infections/Antimicrobial Resistance Program, the State Epidemiologist, and Division of Community and Public Health.

This information is current as of November 30, 2023 but may be modified in the future. We may continue to post updated information regarding the most common questions about this subject.